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Demographic and Illness-Related Variables Associated with HIV-Related Fatigue

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Abstract

Fatigue is one of the most debilitating symptoms suffered by those with HIV infection, yet little is known about its correlates. Our primary aims are to describe the degree to which fatigue affects daily functioning and the demographic and illness-related predictors of fatigue. The sample (n = 128) was composed of primarily poor, unemployed people of color. Fatigue most often interfered with the ability to think quickly, perform household chores, exercise, work, engage in recreational activities, walk, plan activities, and think clearly. The consequences of fatigue were highest for lowered motivation, difficulty concentrating, increased drowsiness, losing patience, and interference with work, family, and social life. Multiple linear regression analyses revealed statistically significant associations of employment status, monthly income, current antidepressant use, and number of years living with HIV infection as predictors of fatigue. These must be better understood in order to develop interventions to successfully ameliorate HIV-related fatigue.

Introduction

Although deaths from HIV infection have dropped dramatically, patients are still dealing with symptoms that interfere with the ability to lead full, productive lives. Fatigue is the most frequent and debilitating complaint of HIV-positive people, with prevalence rates of up to 98% in studies of seropositive individuals (e.g., Anandan, Braveman, Kielhofner, & Forsyth, 2006; Breitbart, McDonald, Rosenfeld, Monkman, & Passik, 1998; Coleman et al., 2006; Duran et al., 2001; Fontaine, Larue, & Lassauniere, 1999; Henderson, Safa, Easterbrook, & Hotopf, 2005; Molassiotis, Callaghan, Twinn, & Lam, 2001; Norval, 2004; Simmonds, Novy, & Sandoval, 2005; Sullivan, Dworkin, & the Adult and Adolescent Spectrum of HIV Disease Investigators, 2003; Vogl et al., 1999; Voss, 2002, 2005). The consequences of fatigue include having to stop working, limiting one's involvement with family and friends, being unable to manage one's finances, and needing an entire day to get through the simplest of household chores (Anandan et al., 2006; Barroso, 2001; Jenkin, Koch, & Kralik, 2006).

With regard to demographic and illness-related variables in studies of HIV-infected individuals, higher fatigue intensity has been reported in women, Hispanics, disabled subjects, those with a lower income, and those with no health insurance (Voss, 2005). Intravenous (IV)

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drug users were found to be more likely to report persistent fatigue than homosexual men (Breitbart et al., 1998; Palenicek et al., 1993). Several researchers have found that women were significantly more likely to report fatigue than men (Breitbart et al.; Mrus, Williams, Tsevat, Cohn, & Wu, 2005). In addition, patients older than age 35 years have reported significantly higher levels of fatigue than younger patients (Singh, Squier, Sivek, Wagener, & Yu, 1997). Patients with more HIV-related symptoms reported more fatigue (Breitbart et al.; Phillips et al., 2004), and efavirenz has been related to increased fatigue (Arendt, 2006).

This paper analyzes baseline data from a longitudinal study of HIV-infected men and women from a community in the southeastern United States. The primary aims of this paper are twofold: 1) to describe the degree to which fatigue impacts daily functioning, and 2) to determine the demographic and illness-related predictors of fatigue.

Methods

Sample

HIV-infected individuals, 21 years of age or older, who could read and speak English and were mentally competent enough to provide reliable data were considered eligible for the study. The Principal Investigator (PI) (second author) evaluated potential participants during a detailed telephone-screening interview for obviously confused or inappropriate remarks that may have indicated some condition, such as dementia or psychosis, that would preclude successful completion of the study. As a doctorally prepared nurse practitioner, the PI was confident that she would be able to determine, during the screening, if there were any problems in mental competence. Both fatigued and non-fatigued persons were enrolled. Persons with a co-morbid condition marked by fatigue, such as renal disease, cancer, or multiple sclerosis, were excluded, as were pregnant women and those women less than 12 months postpartum.

Flyers advertising the study were distributed at HIV/AIDS treatment centers and service organizations in a southeastern state. While fatigue was prominent on the flyer, we stated that we were searching for both fatigued and non-fatigued people. The Institutional Review Board at a major academic medical center approved the study protocol, and written informed consent was obtained from each participant.

Procedures

Persons interested in participating in the study contacted the PI who conducted the preliminary screenings by telephone. Potential participants were then contacted by one of the two study coordinators, and an initial visit was scheduled. The study visits were conducted at the General Clinical Research Center (GCRC) of an academic medical center. Participants were encouraged to take breaks whenever they became tired. Participants were paid $70 for the study visit, which included reimbursement for transportation costs.

Baseline demographic data were collected at the first study visit by one of two research assistants during face-to-face interviews with study subjects. An investigator-developed form was used to collect demographic data, including age, race/ethnicity, employment status, income, medications (including antiretrovirals, antidepressants, and anxiolytics), HIV-related illnesses (categorized into B [symptomatic HIV infection] or C [clinical conditions indicating AIDS] illnesses, using the Centers for Disease Control and Prevention guidelines [CDC, 1992]), other chronic illnesses, care-giving responsibilities/number of children living in the home, recreational drug and alcohol use, and pain status (rated on a 1–10 scale, with 1 being “no pain” to 10 being the “worst pain ever”).

The HIV-Related Fatigue Scale (HRFS) (Barroso & Lynn, 2002) was used to measure several aspects of fatigue. It is a Likert-type, 56-item self-report measure with the following scales:

fatigue intensity (8 items; Cronbach's alpha 0.93) and impact of fatigue on daily functioning (22 items; Cronbach's alpha 0.98), with the latter being divided into three subscales: impact of fatigue on activities of daily living (ADL) (12 items; Cronbach's alpha 0.96), impact of fatigue on socialization (6 items; Cronbach's alpha 0.93), and impact of fatigue on mental functioning (4 items; Cronbach's alpha 0.93). In addition, we examined other individual items on the HRFS that concerned descriptions of fatigue and triggers of fatigue. A higher score on scales and items indicates more intense fatigue or greater adverse impact of fatigue.

Responses ranged from 1–7 or 1–10 depending on the question; the former were rescaled to range from 1–10 before computing summary scales as described below. The HRFS has a 7th grade reading level. Subjects whose intensity of fatigue is low (1 or 2) on all of the first seven HRFS items (e.g., my level of fatigue today; my level of fatigue on most days; how severe is the fatigue) are told to skip the rest of the instrument, since all of the remaining items are dependent on the subjects being fatigued. Therefore, the few subjects in this study with virtually no fatigue (n = 15) were given a 1 on all scales, subscales, and individual items.

Data Analysis

For descriptive purposes we report the fatigue items with the highest means. We fit bivariable and multivariable linear regression models to evaluate the predictors of each fatigue scale. We entered as predictors sex, race, and all other demographic and clinical characteristics that had P values <0.10 in bivariate analyses. We modeled monthly income using a log transformation to reduce the skew in this variable. We assessed all final models for violations of key assumptions, including homoscedasticity and normality of distribution of the dependent variable. We examined residual and leverage statistics to assess whether any individual observations were overly influential in the estimation of each model. We assessed the potential for curvilinear relationships between continuous independent variables and our dependent variables by comparing, for each continuous variable, a model including only a linear term to a model where the continuous variable was represented by a restricted quadratic spline with 5 knots (Harrell, 2001). In all cases, likelihood-ratio tests between the two choices indicated that the simple linear term was appropriate, and linear terms were, therefore, used for all continuous variables. This decision was further supported by visual examination of locally weighted scatterplot smoothing (LOWESS) graphs.

Results

The baseline sociodemographic and clinical characteristics of the study sample are described in Table 1. The majority of subjects were African American (n = 84, 66%), followed by Caucasian (n = 39, 30%); 4% (n = 5) were other ethnic minorities (e.g., Hispanic, Native American). Thirty-four percent (n = 44) of the subjects were female, and the median age was 44 years old. The median number of years of education for this sample was 12. A minority of subjects were employed at baseline (n = 42, 33%), and the median monthly income of the sample was $686. Fifteen percent ($n$ = 19) of the subjects were acting as primary caregivers for someone else, and the median number of household members for the whole sample was two.

The sample was predominantly made up of people who had lived with HIV infection for a long time, median 10 years since diagnosis (range 0–25 years). With regard to HIV-related illnesses, 9% (n = 12) of the subjects had experienced a CDC Category B illness, and 17% (n = 22) had experienced a CDC Category C illness. Current antidepressant and anxiolytic use was reported by 39% (n = 50) and 15% (n = 19), respectively. A large number (n = 105, 82%) of subjects were on antiretroviral therapy at baseline. Many (n = 83, 65%) reported living with at least one other chronic illness (e.g., hypertension, depression, arthritis). A large number of subjects (n = 98, 77%) reported having used street drugs at some point, with 66% (n = 84) reporting having

used drugs stronger than marijuana, and 20% (n = 26) reporting injection drug use. Twenty-two percent (n = 28) reported current street drug use, and 9% (n = 12) reported having a current alcohol problem. At least some pain was reported by 45% (n = 58) of the subjects.

Table 2 presents the mean scores for the various fatigue subscales, with higher scores indicating greater intensity of fatigue or greater adverse impact of fatigue. In terms of individual items on the HRFS (data not shown in table), the mean score for level of fatigue most days was 4.9 (SD = 2.2), and the mean score for fatigue severity in the week prior to the first study visit was 5.6 (SD = 2.8) (responses for each of these is on a 1–10 scale). In an item analysis of the daily functioning scale, we found the highest mean scores (on a 1–10 scale) on fatigue affecting the ability to think quickly (5.1, SD = 3.2), perform household chores (5, SD = 2.8), exercise (5, SD = 3.2), work (4.8, SD = 3.4), engage in leisure and recreational activities (4.8, SD = 3), walk (4.8, SD = 3), plan activities ahead of time (4.8, SD = 3.2), and think clearly (4.8, SD = 3.3). With regard to the descriptive items (on a 1–7 scale), the consequences of fatigue were highest for lowered motivation (5.5, SD = 2.2), difficulty concentrating (5.1, SD = 2.2), increased drowsiness (4.9, SD = 2.3), losing patience (4.7, SD = 2.3), and interference with work, family, and social life (4.7, SD = 2.3). Subjects noted that fatigue was most often exacerbated by stress (4.9, SD = 2.2) or depression (4.7, SD = 2.4). Fatigue was listed as one of the three most disabling symptoms (4.8, SD = 2.3), and it was unpredictable (4.7, SD = 2.3). The fatigue that subjects were currently experiencing was different in quality and severity than the fatigue they experienced before developing HIV (4.7, SD = 2.4).

Baseline demographic and illness-related variables found to be significantly associated with fatigue in bivariate analyses included race/ethnicity, monthly income, employment status, years since diagnosis, the presence of other chronic illnesses, current antidepressant use, and pain (see Table 3). African American subjects scored higher than Caucasian subjects on fatigue intensity; however, the difference was not statistically significant ($p > 0.05$). African American subjects did have significantly higher scores on the impact of fatigue on overall functioning than Caucasian subjects ($p < 0.05$). Subjects who were unemployed had higher fatigue intensity scores ($p < 0.01$), and their fatigue had a greater adverse effect on overall functioning ($p < 0.01$). Subjects reporting at least one other chronic illness at baseline had significantly higher fatigue intensity scores than subjects who did not have any other chronic illness ($p < 0.05$). Although subjects with other chronic illnesses scored higher on the impact of fatigue on overall functioning, the difference was not statistically significant ($p > 0.05$). There was a trend for fatigue intensity scores to be higher in those subjects with current pain ($p > 0.05$). Subjects in pain had a greater effect of fatigue on overall functioning ($p < 0.05$). None of the antiretroviral medications was found to be correlated with fatigue.

Table 4 summarizes multiple linear regression analyses. The most important predictors of fatigue were number of years living with HIV infection, monthly income, and current antidepressant use. Subjects with higher income had less impairment of functioning due to fatigue ($p < 0.01$), less impact of fatigue on performance of ADLs ($p < 0.01$), and lower impact of fatigue on socialization ($p < 0.01$). The length of time since HIV diagnosis was found to be negatively correlated with fatigue intensity and overall functioning; those subjects who had lived longer with HIV infection had lower scores on fatigue intensity ($p < 0.01$) and lower scores on fatigue-related impairment of overall functioning ($p < 0.01$). Subjects who had been living with HIV infection longer also reported less impact of fatigue on performance of ADLs ($p < 0.01$), socialization ($p < 0.05$), and mental functioning ($p < 0.01$).

Other trends included higher scores on fatigue intensity ($p < 0.10$) and higher scores on the impact of fatigue on overall functioning ($p < 0.05$) among subjects who were taking antidepressants. Fatigue-related impairment of overall functioning for subjects taking antidepressants included impairment in performing ADLs ($p < 0.05$), impairment in

socialization ($p < 0.05$), and impairment in mental functioning ($p < 0.01$). Models excluding the 15 non-fatigued subjects demonstrated generally consistent results apart from coefficients for antidepressant use, which were no longer statistically significant.

Discussion

While some of these findings about HIV-related fatigue may seem intuitive, this is the first study to report specific details about how, on a day-to-day basis, fatigue adversely impacts the lives of those who suffer from it. The sample reported here is very similar to the people living with HIV in the southeastern United States and reported in other studies across the United States (Bing et al., 2001; Reif, Geonotti, & Whetten, 2006; Whetten et al., 2005); they are largely poor, unemployed members of minority groups with substance abuse problems. Most were on antiretroviral therapy and had at least one additional chronic illness in addition to HIV infection.

One of the most striking aspects of our sample is the length of time – a median of ten years – these subjects had known of their HIV infection. It is possible that the observed association between longer duration of infection and less often reported fatigue reflects different perceptions of fatigue among those who have been dealing with HIV for a longer time. This might also indicate some accommodation to the disease. It is also possible that the newly diagnosed have more depression, which could in turn lead to greater fatigue; the participants in our study may have developed coping mechanisms during their many years with HIV infection that help them feel less depressed.

It is clear that fatigue is interfering with important aspects of the subjects' lives, including the ability to think quickly and/or clearly, perform household chores, exercise, and work. This has economic implications for people who may not be able to function optimally at work, might not be able to maintain a household, or may not be able to work altogether due to fatigue. Fatigue could also have an adverse impact on those trying to maintain employment, as lowered motivation, difficulty concentrating, and increased drowsiness were troubling consequences of HIV-related fatigue. Related to this was the finding that subjects with a higher income reported less fatigue, which was also found in Voss's 2005 study; this may be because they are able to pay others to do fatiguing activities for them, such as yard work or housekeeping, or it may be because higher paying, white-collar jobs are generally less physically demanding. It may also reflect the fact that those who are not fatigued can work more hours and, therefore, make more money.

Regarding implications for clinical practice, when clinicians are assessing a patient's level of disability and need for personal care services and other in-home assistance, they should be alert to the fact that individuals with HIV-related fatigue may not be able to work and perform simple household chores as effectively as HIV-infected individuals who are not fatigued. Clinicians may be able to predict a greater, more debilitating level of fatigue in individuals who are recently diagnosed, as well as individuals who are of a lower socioeconomic status, and those who are currently being treated with antidepressants.

Those with other chronic illnesses were more fatigued; the relationship of chronic illnesses and HIV is likely to become more complex as people with HIV infection live longer and are more likely to develop other comorbid conditions. Researchers will need to look at the interactions of other chronic illnesses when examining symptoms in those who are seropositive. Among the comorbid illnesses, the most influential is depression; the relationship between fatigue and depression is well-documented. Our finding that subjects on antidepressants were more fatigued was surprising; it is possible that the antidepressants were not working in the intended manner, that fatigue was a side effect of the antidepressants, or that the antidepressants

were not sufficient to lift the symptoms of depression. Alternatively, it may be that those who are taking antidepressants are the most depressed and, thus, the most fatigued.

Limitations of the study should be acknowledged. The self-referral method of recruitment in this study may have introduced selection bias, as individuals experiencing fatigue may have been more likely to respond to study advertisements than those not fatigued; hence, the proportion of fatigued participants in this study may be an overestimate of the prevalence of fatigue among HIV-infected individuals generally. Self-reported measures of fatigue may be subject to measurement error; this error would tend to bias estimates of association toward the null if it were unrelated to other variables included in the model. However, initial psychometric findings on the HIV-Related Fatigue Scale are promising.

We were also unable to determine the direction of the relationship between fatigue and the predictors (e.g., does higher income lead to less fatigue or vice versa). Finally, we have examined multiple independent variables in this study; however, each of them was chosen based on previous research. We could locate no other research that reports on all of these variables in one sample, which we believe to be a strength of this study.

We are continuing to follow this sample for a three year period, to help better understand the correlates of fatigue over time and how fatigue changes during the course of HIV infection. Better understanding of this debilitating symptom will help to develop more effective interventions.

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Table 1

Demographic and Clinical Characteristics of Sample (n = 128)

Characteristic	*N* (%) or Median (IQR)
Age, years (range: 26–66)	44 (38–48)
Female	44 (34.4%)
Race:	
African-American	84 (65.6%)
Caucasian	39 (30.5%)
Other	5 (3.9%)
HIV risk factor:	
MSM	50 (39.1%)
Heterosexual sex	42 (32.8%)
IDU	12 (9.4%)
Other/Multiple/Don't know	24 (18.8%)
Years of schooling (range: 4–20)	12 (12–14)
Monthly income (range: $0–$6,000)	$686 ($504–$1,300)
Employed part/full time	42 (32.8%)
Primary caregiver for another	19 (14.8%)
Number of household members	2 (1–3)
Years since HIV diagnosis (range: 0–25)	10 (6–15)
On any antiretroviral therapy	105 (82.0%)
Any HIV-related illness	
CDC Category B	12 (9.4%)
CDC Category C	22 (17.2%)
Any other chronic illnesses	83 (64.8%)
Current psychotropic medication use	53 (41.4%)
Antidepressant	50 (39.1%)
Anxiolytic	19 (14.8%)
Ever used street drugs	98 (76.6%)
Ever used non-marijuana drugs	84 (65.6%)
Currently using street drugs	28 (21.9%)
Ever injected street drugs	26 (20.3%)
Current alcohol problem	12 (9.4%)
Currently in pain	58 (45.3%)

Note. IQR: Interquartile range (25^{th}–75^{th} percentile). MSM: Men who have sex with men.

IDU: Injection drug use

Table 2

HIV-Related Fatigue (n = 126)

Fatigue scale	*N* (%) or Mean (*SD*)
Fatigued	111 (88.1%)
Fatigue intensity*	6.4 (1.6)
Fatigue-related impairment of functioning*	5.6 (2.1)
Impact of fatigue on ADL*	5.5 (2.1)
Impact of fatigue on socialization*	5.5 (2.3)
Impact of fatigue on mental functioning*	6.1 (2.5)

Note. ADL: Activities of daily living.

*Of those reporting any fatigue.

Table 3

Bivariable Ordinary Least Squares Regression Coefficients Comparing Demographic and Clinical Characteristics with HIV-Related Fatigue[a] (n = 126)

Characteristic	Fatigue intensity	Fatigue-related impairment of functioning	Fatigue-related impairment subscales		
			Impact on ADL	Impact on socialization	Impact on mental functioning
Age	0.00	0.01	0.02	−0.02	0.03
Female sex	0.46	0.35	0.39	0.20	0.44
Minority race/ethnicity	0.68	1.10*	1.27**	0.91+	0.86
Risk factor: MSM	−0.48	−0.28	−0.38	−0.09	−0.27
Years of education	−0.14+	−0.16+	−0.15+	−0.16+	−0.17+
Monthly income (log-transformed)	−0.69**	−1.00**	−1.03**	−1.08**	−0.80**
Currently unemployed	1.15**	1.43**	1.50**	1.30**	1.42**
Years since HIV diagnosis	−0.09**	−0.10*	−0.09*	−0.10*	−0.10*
On ART	−1.02*	−0.77	−0.71	−0.99	−0.59
Category C illness	0.15	0.28	0.43	0.00	0.23
Any other chronic illness	0.81*	0.58	0.58	0.45	0.79
Current antidepressant use	0.89*	1.14**	1.10*	1.00*	1.47**
Current anxiolytic use	−0.30	0.25	0.18	0.28	0.37
Current drug use	0.21	0.12	0.19	−0.09	0.24
Current alcohol problem	0.66	0.82	0.95	0.96	0.24
Currently in pain	0.69+	1.04*	1.04*	0.85+	1.30**

** $p < 0.01$,

* $p < 0.05$,

+ $p < 0.10$

Note. ADL: Activities of daily living. MSM: Men who have sex with men. ART: Antiretroviral therapy.

[a] Coefficients are from separate regression models that each include a single independent variable.

Table 4

Multiple Linear Regression Predicting HIV-Related Fatigue (n = 118)

Predictor	Fatigue intensity	Fatigue-related impairment of functioning	Fatigue-related impairment subscales		
			Impact on ADL	Impact on socialization	Impact on mental functioning
Female sex	−0.18	−0.42	−0.33	−0.49	−0.18
Minority race/ethnicity	−0.17	0.19	0.32	0.06	−0.20
Monthly income, log-transformed	−0.33	−0.61**	−0.71**	−0.74**	−0.42
Currently unemployed	0.87+	0.75	0.61	0.59	0.71
Years since HIV diagnosis	−0.12**	−0.12**	−0.11**	−0.11*	−0.15**
On ART	−0.78	−0.50		−0.72	
Category C illness			0.73		0.45
Any other chronic illness	0.59	0.34	0.50		0.70
Current antidepressant use	0.78+	1.11*	0.98*	1.02*	1.44**
Current alcohol problem		0.25	0.31	0.34	
Currently in pain	0.13	0.39	0.42	0.21	0.75
Constant	7.37**	6.89**	6.37**	7.82**	6.35**
R-squared	0.249	0.305	0.322	0.259	0.248

** $p < 0.01$,

* $p < 0.05$,

+ $p < 0.10$

Note. ADL: Activities of daily living. ART: Antiretroviral therapy.